

Studies on 4-Thiazolidinones. Part-VIII. Preparation and Antimicrobial Activity of 2-Aryl-3-acridin-9-yl-amino-5-methyl/carboxymethyl-4-thiazolidinones

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Some new 4-thiazolidinones have been prepared bearing 9-aminoacridine moiety by the condensation of Schiff bases from 9-hydrazinoacridine with thiolactic and thiomalic acids. The structures of the product have been characterised by ir spectral study. The products have been screened for antimicrobial activity, and most of which showed moderate activity.

4-Thiazolidinone derivatives¹ and acridine derivatives² possess diverse biological activities. In continuation of our work on 4-thiazolidinone derivatives³, we have undertaken the synthesis of 4-thia-

zolidinones of type (4) by the condensation of 9-chloroacridine with hydrazine hydrate to yield 9-hydrazinoacridine (2) which on condensation with different aromatic aldehydes gave the Schiff bases (3). 3 on further treatment with thiolactic and thiomalic acids gave substituted-4-thiazolidinones (4). The structure of 4 has been characterised by ir spectral study. The products have been screened for antimicrobial activity.

Antimicrobial activity: The compounds were screened for antibacterial and antifungal activity using cup-plate method⁴. The testing was carried out at a concentration of 50 µg ml⁻¹. Using gram+ve (*Staphylococcus aureus* and *Staphylococcus citreus*) and gram-ve bacteria (*Escherichia coli* and *Marcasane serratia*) and fungi (*Aspergillus niger* and *Saccharomyces cerevisiae*). It was observed that most of the compounds were moderately active (16-28 mm zone of inhibition) against different strains of bacteria and fungi.

However, comparatively significant activity was observed in compounds bearing (zone of inhibition in mm) X=CH₃ and R=Ph (19-28), 3-aminophenyl (16-24), 2-nitrophenyl (22-28), 4-methoxyphenyl (20-26), 2,6-dichlorophenyl (18-30 mm), and when X=CH₂COOH and R=2-chlorophenyl (15-28), 3-aminophenyl (16-23), 2-nitrophenyl (15-21), 4-dimethylaminophenyl (15-20 mm), respectively.

Experimental

M.ps. were determined in open capillaries and are uncorrected. The ir spectra (KBr) was taken on a Shimadzu DR-1 435-IR spectrophotometer.

9-Benzal hydrazinoacridine: Benzaldehyde (0.01 mol, 1.06 g) was condensed with 9-hydrazinoacridine (0.01 mol, 2.09 g) in methanol (20 ml) at 70-80° for 3 h. The resulting solid was isolated and crystallised from ethanol, (65%), m.p. 69° (Found: C, 80.79; H, 5.00; N, 14.08. C₂₀H₁₅N₃ calcd. for: C, 80.80; H, 5.05; N, 14.14%); ν_{max} (KBr) 3 350 (NH str), 1 620 (C=N str) and 760 cm⁻¹ (N-H wag).

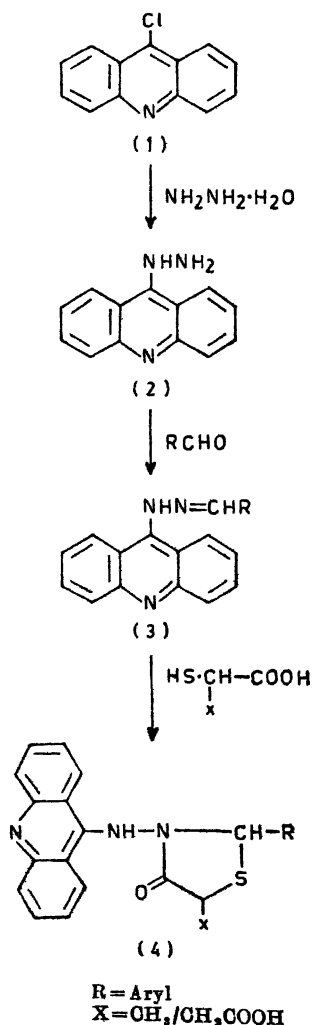


TABLE 1—PHYSICAL AND ANALYTICAL DATA OF COMPOUNDS 3 AND 4

R	Schiff base (3)		Thiazolidinones (4)			
	M.p. °C	N%, Found (Calcd.)	M.p. °C	X=OH, N%, Found (Calcd.)	M.p. °C	X=OH,COOH N%, Found (Calcd.)
Phenyl	69	14.08 (14.14)	93	10.83 (10.90)	144	9.76 (9.79)
2-Chlorophenyl	125	12.62 (12.68)	110	10.00 (10.02)	143	9.03 (9.07)
4-Chlorophenyl	143	12.60 (12.68)	98	9.86 (10.02)	168	9.05 (9.07)
2,4-Dichlorophenyl	103	11.43 (11.50)	140	9.22 (9.27)	103	8.42 (8.45)
2,6-Dichlorophenyl	117	11.45 (11.50)	132	8.93 (9.27)	189	8.41 (8.45)
3,4-Dichlorophenyl	83	11.41 (11.50)	105	9.00 (9.27)	262	8.43 (8.45)
3-Aminophenyl	92	17.90 (17.94)	108	10.82 (10.88)	235	9.70 (9.76)
4-Aminophenyl	78	17.85 (17.94)	112	10.83 (10.88)	163	9.73 (9.76)
2-Nitrophenyl	110	16.33 (16.37)	124	12.98 (13.02)	248	11.78 (11.81)
3-Nitrophenyl	219	16.30 (16.37)	157	13.00 (13.02)	180(D)	11.80 (11.81)
4-Nitrophenyl	172	16.32 (16.37)	167	12.98 (13.02)	195	11.68 (11.81)
2-Hydroxyphenyl	75	13.38 (13.41)	118	10.41 (10.47)	252	9.40 (9.43)
4-Hydroxyphenyl	140	13.39 (13.41)	98	10.44 (10.47)	147	9.38 (9.43)
2-Methoxyphenyl	208	12.80 (12.84)	100	10.08 (10.12)	228	9.13 (9.15)
3-Methoxyphenyl	86	12.83 (12.84)	130	10.10 (10.12)	252	9.10 (9.15)
4-Methoxyphenyl	120	12.78 (12.84)	148	10.06 (10.12)	268	9.11 (9.15)
3,4-Dimethoxyphenyl	75	11.70 (11.76)	103	9.40 (9.43)	123	8.53 (8.58)
3-Methoxy-4-hydroxyphenyl	87	12.00 (12.24)	114	9.68 (9.74)	132	8.80 (8.84)
4-Dimethylaminophenyl	105	15.48 (16.47)	118	13.00 (13.08)	116	11.82 (11.86)
Cinnamyl	85	12.58 (13.00)	122	10.18 (10.21)	147	9.20 (9.23)

Similarly, other substituted Schiff bases were prepared (Table 1).

2-Aryl-3-acridin-9-ylamino-5-methyl-4-thiazolidinones : A mixture of thiolactic acid (0.01 mol, 1.06 g) and 9-benzalhydrazinoacridine (0.01 mol, 2.97 g) was refluxed on a oil-bath for 6 h. The solid product was isolated by washing the upper organic layer with sodium bicarbonate solution and water, and crystallised from methanol, (73%), m.p. 93° (Found : C, 71.35 ; H, 4.91 ; N, 10.83 ; S, 8.20. $C_{23}H_{19}N_3OS$ calcd. for : C, 71.68 ; H, 4.93 ; N, 10.90 ; S, 8.31% ; ν_{max} (KBr) 3 350 (NH str), 1 720 (C=O str), 1 590 (C=N str) and 700 cm^{-1} (CSC str).

Similarly, the other 4-thiazolidinones were prepared (Table 1).

2-Aryl-3-acridin-9-ylamino-5-carboxymethyl-4-thiazolidinones : A solution of 9-benzalhydrazinoacridine (0.01 mol, 1.06 g) in dry benzene (10 ml) was added to thiomalic acid (0.01 mol, 1.51 g) and the mixture refluxed on a oil-bath for 5 h. The solid product was isolated as above and crystallised from ethanol,

(78%), m.p. 144° (Found ; C, 67.00 ; H, 4.38 ; N, 9.76 ; S, 7.39. $C_{24}H_{19}N_3O_2S$ calcd. for : C, 67.13 ; H, 4.42 ; N, 9.79 ; S, 7.46% ; ν_{max} (KBr) 3 425 (OH str), 3 300 (NH str), 1 310 (O=C-O str), 1 690 (C=O str) and 690 cm^{-1} (CSC str).

Similarly, other substituted-4-thiazolidinones were prepared (Table 1).

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